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Published in:
Book of Abstracts, Sustain 2017

Publication date:
2017

Document Version
Publisher's PDF, also known as Version of record

Impact of physiological shear stress on cell association/uptake with a novel multicompartment carrier

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The development of multicomparment carriers is an increasingly expanding area of research due to the numerous advantages offered over classical drug delivery vehicles. In particular, a compartmentalized structure guarantees the co-localization of several (incompatible) drugs at the target site by encapsulating each drug in separated compartments within the same carrier.[1]

From a different perspective, despite the extensive research over several decades on the development of drug delivery vehicles, only a handful of platforms have reached either clinical trials or the market.[2] This fact evidences an underlying poor transition from traditional *in vitro* to *in vivo* studies. A potential solution would be to make use of *in vitro* set ups that better mimic the human physiology thus resulting in a reduction of expensive and complex animal studies along with an experimental outcome more relatable to *in vivo* experiments. Several studies have demonstrated that the mechanical forces, such as shear stress, generated by the dynamics of the human physiology, i.e blood flow or interstitial fluid flow in tumors, highly impact the cell-carrier interaction in terms of cytotoxicity, targeting efficiency, etc.[3]

Aiming to demonstrate the impact of physiological shear stress on the cell-carrier interaction, we developed a novel multicompartment carrier with a functionalized surface to achieve stealth carriers (less cellular uptake) to which three relevant cell lines, i.e macrophages, endothelial and cancer cells, were exposed under the presence or absence of shear stress mimicking the physiological conditions of veins, capillaries and tumors.

Our results demonstrated that the cell-carrier association or uptake of the functionalized or non-functionalized carrier is highly dependent on the presence or absence of shear stress, the intensity of the shear stress as well as on the cell line. Different results were obtained in terms of the efficacy of the coating. Thus, shear stress should be considered when developing a drug delivery vehicle by including it in *in vitro* set ups using microfluidic devices.

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